

WHAT IS CLAIMED IS:

1. A polypeptide comprising a granulocyte colony stimulating factor (G-CSF) domain operably linked to a transferring (Tf) domain,
5 wherein the ability of the polypeptide to be transported into a cell expressing a transferring receptor (TfR) gene or the ability of the polypeptide to be transported across a cell expressing a TfR gene via transcytosis is higher than that of the G-CSF domain alone.
2. The polypeptide of claim 1, wherein the G-CSF domain and
10 the Tf domain are linked through non-covalent bonding.
3. The polypeptide of claim 1, wherein the G-CSF domain and the Tf domain are linked through covalent bonding.
4. The polypeptide of claim 3, wherein the G-CSF domain and the Tf domain are linked through a disulfide bond.
- 15 5. The polypeptide of claim 3, wherein the polypeptide is a recombinant polypeptide.
6. The polypeptide of claim 5, wherein the G-CSF domain is linked to the Tf domain through a linker.
7. The polypeptide of claim 6, wherein the G-CSF domain is
20 linked to the Tf domain through a Leu-Glu linker.
8. The polypeptide of claim 5, further comprising a secretion signal at the N-terminus.
9. The polypeptide of claim 5, wherein the order of the G-CSF domain and the Tf domain is from the N-terminus to the C-terminus.
- 25 10. The polypeptide of claim 1, wherein the Tf domain comprises at least one iron molecule.
11. The polypeptide of claim 10, wherein the Tf domain comprises two iron molecules.
12. A nucleic acid comprising a DNA sequence encoding the
30 polypeptide of claim 5 or 9.

13. A cell comprising the nucleic acid of claim 12.
14. A composition comprising a pharmaceutically acceptable carrier and the polypeptide of claim 1, 4, 5, or 9.
15. The composition of claim 14, further comprising sodium bicarbonate, BSA, casein, or a combination thereof.
16. A composition comprising a pharmaceutically acceptable carrier and the nucleic acid of claim 12.
17. A method of producing a polypeptide, comprising cultivating the cell of claim 13 under conditions that allow expression of the polypeptide.
18. The method of claim 17, further comprising collecting the polynucleotide.
19. A method of enhancing transport of G-CSF into or across a GI epithelial cell, comprising contacting a GI epithelial cell with the polypeptide of claim 1 under conditions that allow transport of the polypeptide into the cell through TfR or transport of the polypeptide across the cell through TfR via transcytosis.
20. A method of enhancing transport of a polypeptide into or across a GI epithelial cell, comprising contacting a GI epithelial cell with a polypeptide operably linked to a Tf domain under conditions that allow transport of the Tf-linked polypeptide into the cell through TfR or transport of the Tf-linked polypeptide across the cell through TfR via transcytosis, wherein the molecular weight of the polypeptide is at least 10 kD, the size of the Tf-linked polypeptide is no more than 200 nm, and the ability of the Tf-linked polypeptide to be transported into a cell expressing a TfR gene or the ability of the Tf-linked polypeptide to be transported across a cell expressing a TfR gene via transcytosis is higher than that of the polypeptide alone.
21. The method of claim 20, wherein the molecular weight of the polypeptide is at least 15 kD.

22. The method of claim 21, wherein the molecular weight of the polypeptide is at least 20 kD.

23. A method of enhancing transport of a polypeptide into or across a GI epithelial cell, comprising contacting a GI epithelial cell with
5 a recombinant protein containing a polypeptide operably linked to a Tf domain under conditions that allow transport of the Tf-linked polypeptide into the cell through TfR or transport of the Tf-linked polypeptide across the cell through TfR via transcytosis, wherein the ability of the Tf-linked polypeptide to be transported into a cell
10 expressing a TfR gene or the ability of the Tf-linked polypeptide to be transported across a cell expressing a TfR gene via transcytosis is higher than that of the polypeptide alone.

24. The method of claim 23, wherein the polypeptide includes a G-CSF domain.

15 25. A method of enhancing production of circulating neutrophils in a subject, comprising administering to a subject in need thereof an effective amount of the composition of claim 14.

26. The method of claim 25, wherein the subject is undergoing chemotherapy for cancer, or is suffering from or at risk for developing
20 severe chronic neutropenia or a bone marrow transplant-related disorder.

27. The method of claim 25, wherein the composition is administered orally.

28. The method of claim 25, wherein the composition is
25 administered subcutaneously.

29. A method of enhancing production of circulating neutrophils in a subject, comprising administering to a subject in need thereof an effective amount of the composition of claim 16.

30. The method of claim 29, wherein the subject is undergoing
30 chemotherapy for cancer, or is suffering from or at risk for developing

severe chronic neutropenia or a bone marrow transplant-related disorder.